

REMARKS

Reconsideration and reexamination of the subject application are respectfully requested in light of the foregoing amendments and following remarks.

1. Change of Correspondence Address

The correspondence address for this application has changed. The Revocation and New Power of Attorney filed herewith designates practitioners associated with Customer Number 55694 to prosecute this application and to transact all business in the Patent and Trademark Office connected herewith. Accordingly, the new correspondence address is:

DRINKER BIDDLE & REATH LLP
Suite 1100
1500 K Street, N.W.
Washington, DC 20005-1209

2. Status of the Claims

Claims 1-17 and 19-27 are pending in the application. Claims 7-10, 13, 16, 17, and 25-27 are withdrawn. Claims 25-27 are canceled by entry of the present amendment for the sole purpose of expediting prosecution. The claims are canceled without disclaimer of any subject matter and without prejudice to Applicants' right to pursue the canceled subject matter in a later filed divisional application. Claims 1-6, 11-12, 14-15, and 19-24 are pending reconsideration and reexamination.

3. Support for the Amendments

Claim 1

Claim 1 is amended to incorporate the elements of Claim 20. The incorporated language is further amended to clarify that the at least one ligand for which the chemical identity is determined is the same at least one ligand that binds the entity that exhibits the detected activity. The specification describes this embodiment of the invention at Example 3, for instance, particularly at page 16, line 10.

To expedite prosecution, Claim 1 is further amended to clarify the antecedent basis for two terms in part (iv) of the claim and to correct obvious inconsistencies in punctuation.

New Claim 28

Claim 28 provides that part (i) of Claim 1 comprises providing a plurality of different ligands, wherein multiple copies of each different ligand are attached to a separate support to form a plurality of ligand-support complexes, wherein each support is attached to multiple copies of a different ligand. In this embodiment, every support, e.g., a bead, contains multiple copies of the same ligand, and every support also contains a different ligand.

Support for this new claim is provided throughout the specification. *See, e.g.*, Specification, ¶ 21 (describing the “split, couple, recombine method” of Furka *et al.*, *Int. J. Peptide Protein Res.* 37: 487-93 (1991); Lam *et al.*, *Nature* 354: 82-84 (1991); WO 92/00091; U.S. Patents No. 5,010,175, No. 5,133,866, and No. 5,498,538, which produce a library in which “multiple copies of a single ligand are synthesized on each particle (e.g., bead)”; ¶ 4 (characterizing some of the aforementioned references as producing libraries in which “[e]ach bead essentially has millions of copies of a single structure on its surface and different beads contain different sequences”); Examples 3, 5, and 6.

4. Election/Restriction and Request for Rejoinder

Claims 25-27 are withdrawn from consideration as directed to non-elected inventions. Claims 25-27 are canceled by entry of the present amendment without disclaimer or prejudice to Applicants’ right to pursue these claims in a timely filed divisional application.

Claims 7-10, 13, and 16-17 are withdrawn as directed to non-elected species. Applicants appreciate the rejoinder of species directed to (1) species of ligands, (2) species of supports, and (3) species of entities. Pursuant to item 10 of the Office Action mailed January 11, 2006, Applicants respectfully request timely rejoinder of the withdrawn claims, directed to the non-elected species of (1) mixtures/compositions and (2) activities, upon indication of allowance of a generic claim that encompasses the species.

5. Objection to the Specification

The Office objects to the specification because HPQFLS in the second to last line of paragraph 62 requires a sequence identifier. The objection is mooted by the present amendment of the specification.

6. Rejection Under 35 U.S.C. § 112, Second Paragraph

Claims 1-6, 11-12, 14-15, and 19-24 are rejected under 35 U.S.C. § 112, second, as allegedly indefinite. Specifically, the Office implies that “complex,” as used in the claims, is an adjective, referring a degree of complexity of the recited method. As such, the Office then alleges that “complex” is a relative term that is not defined in the specification.

Applicants traverse the rejection.

During the prosecution of a patent application, definiteness of the claim language must be analyzed in light of the teachings of the prior art and the specification as it would be interpreted by one possessing ordinary skill in the pertinent art. *In re Moore*, 439 F.2d 1232, 1235, 169 U.S.P.Q. 236, 238 (C.C.P.A. 1971). In the present case, at each occurrence of “complex” in the claims, the term is used as a noun, not an adjective. The artisan of ordinary skill thus would understand that the term refers to a complex (noun), not that a particular recited claim element is complex (adj.) in nature. The Office has provided no objective evidence on the record that the artisan would understand the term otherwise, as the Office must to establish a *prima facie* case of indefiniteness. Because “complex” is used as a noun and not an adjective, the term does not refer to a degree of complexity of the recited method; therefore, the issue of whether the term is indefinite on this basis is moot.

Accordingly, the rejection is improper and should be withdrawn.

7. Rejection Under 35 U.S.C. § 102(b)

Claims 1-5 and 11-12 are rejected under 35 U.S.C. § 102(b) as allegedly anticipated by Baumbach *et al.*, “Protein purification using affinity ligands deduced from peptide libraries,” *BioPharma* May: 24-31 (1992) (“Baumbach”). Applicants traverse the rejection as it applies to the amended claims.

The Office acknowledges that Baumbach does not teach the subject matter of Claim 20. Claim 1 is herein amended to incorporate this subject matter. Accordingly, Baumbach does not teach all the elements of the claimed invention, and the rejection may be withdrawn.

8. Rejection Under 35 U.S.C. § 103(a)

Claims 1-6, 11-12, 14-15, and 19-24 are rejected under 35 U.S.C. § 103(a) as allegedly obvious over Huang *et al.*, “Simultaneous detection of multiple cytokines from conditioned media and patient’s sera by an antibody-based protein array system,” *Anal. Biochem.* 294: 55-62 (July 1, 2001) (“Huang”) in view of U.S. Patent No. 5,510,240 (“Lam”). Applicants traverse the rejection as it applies to the amended claims.

A. The legal standard for determining obviousness

Whether a claim is obvious is based on an objective analysis of the scope and content of the prior art, the differences between the prior art and each element of the claimed invention, and the level of skill in the pertinent art. *See Graham v. John Deere Co.*, 383 U.S. 1, 15-17 (1966). The Office’s objective analysis of obviousness must be made explicit. *See KSR Int’l Co. v. Teleflex, Inc.*, 82 U.S.P.Q.2d 1385, 1396 (2007); *In re Kahn*, 441 F.3d 977, 988 (Fed. Cir. 2006) (“[R]ejections on obviousness grounds cannot be sustained by mere conclusory statements; instead, there must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness”). The factual inquiry whether to combine references must be based on objective evidence of record. *In re Lee*, 277 F.3d 1338, 1343 (Fed. Cir. 2002) (“This precedent has been reinforced in myriad decisions, and cannot be dispensed with.”). In short, the factual question of motivation cannot be resolved on the basis of subjective belief. *See Lee*, 277 F.3d at 1343-44.

B. Huang

The Office admits that Huang does not disclose detecting an activity of the entity other than binding. Office Action, page 7. Huang further neither teaches nor suggests step (vii) of Claim 1, namely, “determining the chemical identity of at least one ligand to which said entity that exhibits the detected activity binds.” Indeed, Huang already knows the identity of the antibodies (i.e., ligands) attached to a support. It is precisely the knowledge of the identity of the antibody that allows Huang to determine the identity of the cytokines (i.e., entities) bound to the ligand-support complex. For example, Huang identifies cytokines in a mixture by the binding of a particular cytokine to its cognate capture antibody. *See, e.g.*, Huang, Figure 2. The method of Huang would be inoperative if the artisan did not know the identity of the capture antibodies. The presently claimed invention, by contrast, uses a ligand that is not identified until step (vii).

C. Lam

The deficiencies of Lam are noted in Applicants' response filed April 5, 2007. Applicants' response is incorporated herein in its entirety by reference and repeated verbatim for clarity of the record.

Lam differs from claim 1 (step iv), because Lam assays the activity of the ligand, not the acceptor molecule as required by claim 1. *See, e.g.*, Lam, column 2, lines 35-36, stating the bio-oligomers may catalyze a chemical reaction; *see also* lines 32-35, stating the bio-oligomers characterize ligands capable of binding to acceptor molecules or mediating a biological activity of interest. Lam simply does not teach assay of the activity of the **entity**, a recited and required element of claim 1 (step iv), because Lam employs a predetermined entity (acceptor molecule) having a predetermined activity.

Lam also does not teach or suggest "assaying the activity of the entity wherein the entity may be dissociated partially or completely from an entity-ligand-support complex separated in step (iii)). . . ." a required element of claim 1 (step iv). Lam assays the binding of the bio-oligomer to the acceptor molecule and assays the bio-oligomer for an activity of interest, whereas in contrast, the claimed invention assays the binding and assays the activity of the entity dissociated partially or completely from the entity-ligand-support complex.

Claim 1 (step vi) further recites "selecting . . . the entity-ligand-support complex that bound the entity that exhibited the detected activity." In Lam, each bio-oligomer species to which the acceptor molecule binds is found on a single solid phase support so that the support, and thus the bio-oligomer, can be readily identified and isolated (column 17, lines 57-60). Lam thus differs from the claim element because Lam selects the acceptor-bio-oligomer-support based on the activity of the bio-oligomer, not on the basis of the entity that exhibited the detected activity as required in claim 1 (step vi) of the claimed invention.

D. The combination of Huang and Lam

The presently claimed invention is directed to a method of screening a mixture for active entities, comprising in part:

- (vi) selecting at least one entity-ligand-support-complex that bound the entity that exhibited the detected activity; and
- (vii) determining the chemical identity of at least one ligand to which said entity that exhibits the detected activity binds,

whereupon a mixture is screened for active entities.

Huang, in short, identifies an entity of interest in a mixture by determining which antibody of known specificity binds the entity. Huang already knows the chemical identity of the antibodies; therefore, Huang does not determine the chemical identity of at least one ligand to which the entity that exhibits the detected activity binds, as claimed. Lam, on the other hand, assays the bio-oligomer (i.e., ligand) for an activity of interest, but Lam does not select at least one entity-ligand-support-complex that bound the entity that exhibited the detected activity, as claimed. Instead, as set forth above, Lam already knows the identity of the entity.

A modification of Huang in view of Lam, as proposed by the Office, would require Huang to use ligands of unknown chemical identity. This modification would make the method of Huang inoperative, because Huang uses the antibodies of known specificity to identify the entities of interest. Lam does not cure this deficiency, because the method of Lam requires the use of a known entity to identify the bio-oligomer ligand. The Office provides no objective evidence on the record—as it must—to support the allegation that the artisan of ordinary skill would have been motivated to make these modifications at the time of the invention in light of the teachings of the combined references. *See, e.g., KSR*, 82 U.S.P.Q.2d at 1396; *Kahn*, 441 F.3d at 988; *Lee*, 277 F.3d at 1343-44. The rejection accordingly should be withdrawn.

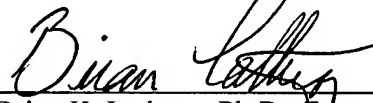
CONCLUSION

In conclusion, this amendment and reply is believed to be a full response to the outstanding Office Action. Should any issues remain outstanding or if there are any questions concerning this paper, or the application in general, the Examiner is invited to telephone the undersigned representative at the Examiner's earliest convenience.

If there are any other fees due in connection with the filing of this response, please charge the fees to our Deposit Account No. 50-0573. If a fee is required for an extension of time under 37 C.F.R. § 1.136 not accounted for above, such an extension is respectfully requested and the fee should also be charged to our Deposit Account.

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Respectfully submitted,



Brian K. Lathrop, Ph.D., Esq.
Registration No. 43,740
DRINKER BIDDLE & REATH LLP
1500 K Street, N.W., Suite 1100
Washington, D.C. 20005-1209
Tel: (202) 842-8862
Fax: (202) 204-0289